

carries no net charge, the dipeptide having at least 2 pKa's which are separated by no more than about 3.5 pH units , the solution having a pH which is within [about] 1.0 pH unit of the isoelectric pH.

A clean copy of the amended claim is attached hereto as Appendix A.

## **REMARKS**

### **I. New Oath**

The Applicants respectfully point out that this Application has been granted Rule 1.47(a) status pursuant to our petition filed concurrently with the present application. A copy of the petition response dated 07 July 1999 is attached hereto as Exhibit A.

### **I. Rejection Under § 112**

The Examiner has rejected claims 1-8 as being indefinite for failure to particularly point out and distinctly claim the subject matter which Applicant regards as the invention because the claims refer to "drug or electrolyte". The Examiner further asserts that the terms are mutually exclusive.

Applicant's assert that the terms are each clearly defined in their own right and the Examiner has put forth no basis for a requirement that the terms be mutually exclusive. This situation is unlike *Ex part Wu*, in that one term is not all inclusive within the other.

In the second paragraph on page 7 of the current office action, the Examiner asserts that "drug" is the broad recitation and "electrolyte" is the narrow recitation. However, the Examiner in paragraph 10A has already indicated that some drugs are electrolytes and some electrolytes

(and therefore not ALL electrolytes) are drugs, so clearly “electrolytes” cannot be a narrower category of drugs.

Further on page 8 of the specification, the difference between the use of the term drug and electrolyte for this application is given:

*“The reservoir formulation may be a donor reservoir formulation containing a drug or other therapeutic agent to be transdermally delivered. Alternatively, the reservoir formulation may be a counter reservoir formulation containing an electrolyte (e.g. saline).”*

Generally electrotransport devices have two electrodes and one or two reservoirs. If the reservoir formulation is for use in an active reservoir then the claims refer to a drug. If the formulation is for a counter reservoir then the electrolyte is not a drug, and usually an inorganic salt such as NaCl.

The specification further defines on page 9 that the term dipeptide is “any polypeptidic chain of 2-5 amino acid residues long.”

In paragraph 10C, the Examiner has requested clarification of the term dipeptide buffer. As currently configured, claim 1 recites “..comprising an aqueous solution of a drug or an electrolyte and a dipeptide buffer, ...”. The claim recites the open ended term “comprising” which clearly provides for the possibility of additional ingredients beyond the recited drug or electrolyte and the dipeptide which is functioning as a buffer.

In paragraph 10D, the Examiner asserts that claim 1 “*lacks metes and bounds since the pK of a given dipeptide will vary given the particular selected dipeptide and the experimental condition for measuring pH. Accordingly, defining the dipeptide by its pKA lacks metes and bounds since the claim neither recites the conditions present for determining pH[sic] or the particular dipeptide.*”

Applicant's disagree. The pKa's for an amino acid or peptide is essentially a series previously determined constant(s) for any particular peptide or amino acid. The determinations of the pKa's are done under specific universally recognized conditions and the values obtained are so recognized by those skilled in the art as referring to measurements determined under these conditions. For an amino acid with hydrocarbon R-groups, such as valine and glycine, there will be two pKa's. For amino acids such as glutamic and aspartic acid, there are three pKa's. For a dipeptide such as Asp-Glu, there would be 4 pKa's, two side-chain carboxyl, one amino group and the alpha-carboxyl group. Applicants include several pages from BIOCHEMISTRY, by Lehninger, attached hereto as exhibit B. These pages show the titration curve for alanine, glutamic acid, lysine and histidine. Referring in particular to the titration curve for glutamic acid, there are three inflection points which reflect the pKa's for the two carboxyl groups and the amine group.

Applicant's admit that different amino acids and different dipeptides could have different pKa values, but that can't be a basis for a § 112 rejection. That is equivalent to objecting to a claim reciting a range of molecular weights for a compound because the claims didn't recite a particular compound having a specific molecular weight!

In paragraph 10E the Examiner asserts "the phrase 'dipeptide is present ... at a concentration of at least 10mM' is indefinite since the solution volume which is necessary for determining the concentration of dipeptide e.g. (mMoles/liter) is not present in the claim."

Applicant wishes to point out the cited term "mM" is an accepted abbreviation for the term millimolar, which by its definition includes a reference to volume. A copy of the appropriate page from Stedman's Medical Dictionary, 25<sup>th</sup> edition is attached hereto as Exhibit C.

### **B. Rejection under 35 USC § 102(b)**

The Examiner has rejected claims 1-2, and 4-7 under 35 U.S.C. § 102(b) as being anticipated or in the alternative being prima facie obvious over Stover et al., J. Chromatography Vol. 470 (5/89) pages 241-250.

The Applicant has amended the claims so that there is no longer a recitation to an electrolyte, only to a drug. Stove cites no examples of a formulation which included the recited buffers along with a drug. Therefore Stover does not anticipate the Applicant's invention

Further, because Stover is dealing with separation of various heptapeptides using a capillary zone electrophoresis system and one would not be drawn to including a drug in such a formulation.

In addition, Applicants have amended the claims by canceling the word "about". Therefore the cited pH range no longer anticipates or is made obvious by Stover

Applicant respectfully request the withdrawal of the § 102 rejection over Stove.

### **C. Rejection under § 102(b) or § 103(a) over Sorensen**

The Examiner has rejected claims 1-8 as being anticipated by or in the alternative obvious over Sorensen, WO 93/12812.

Claim 1 has been amended so that the cited pH of 6.5 in Sorensen no longer falls within the range of Applicant's claims. Nothing in Sorensen would like one skilled in the art to deviate from the cited pH used by Sorensen.

Applicants respectfully request the withdrawal of the § 102(b) and § 103(a) rejection

**D. Rejection under § 102(a), § 102(b) or § 103(a) over Bjorn**

The Examiner has rejected claims 1-8 as being anticipated by or in the alternative obvious over Sorensen, WO 97/39768.

Claim 1 has been amended so that the cited pH of 6.5 in Bjorn no longer falls within the range of Applicant's claims. Nothing in Bjorn would lead one skilled in the art to deviate from the pH used by Bjorn.

Applicants respectfully request the withdrawal of the § 102(b) and § 103(a) rejection

Because all rejections have been traversed by amendment or arguments, Applicants respectfully assert that the claims are in condition for allowance, notice of which is earnestly solicited.

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